UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/813,331	03/29/2004	Bill J. Peck	10031531-1	5115

22878 7590 07/21/2008

AGILENT TECHNOLOGIES INC.
INTELLECTUAL PROPERTY ADMINISTRATION,LEGAL DEPT.
MS BLDG. E P.O. BOX 7599
LOVELAND, CO 80537

EXAMINER	
WILDER, CYNTHIA B	

ART UNIT	PAPER NUMBER
1637	

NOTIFICATION DATE	DELIVERY MODE
07/21/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

IPOPS.LEGAL@agilent.com

Office Action Summary	Application No.	Applicant(s)	
	10/813,331	PECK ET AL.	
	Examiner	Art Unit	
	CYNTHIA B. WILDER	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 March 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *17-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed August 12, 2004 is acknowledged and has been entered. Claim 1 has been amended. Claim 3 has been canceled. Claims 1-2, 4-28 are pending. Claims 17-28 are withdrawn from consideration as being drawn to a non-elected invention. All of the arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons discussed below. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims.

This action is made FINAL.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Previous Rejections

3. The prior art rejections under 35 USC 103(a) as being unpatentable over Anderson et al in view of Schleifer (A) or Schleifer (B) is withdrawn in view of Applicant's amendments and arguments. The prior art rejection under 35 USC 103(a) as being unpatentable over Anderson et al in view of Schleifer (A), Schleifer (B) and further in view of Blanchard et al is withdrawn in view of Applicant's amendment and arguments. The prior art rejection under 35 USC 102 as being anticipated by Bass et al is maintained and discussed below. The prior art rejection Under 35 USC 103 as being anticipated by Bass et al in view of Anderson et al is maintained and discussed below.

Claim Rejections - 35 USC § 102

4. Claims 1, 16 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Bass (US 6,420,180 B1, July 16, 2002). Regarding claim 1, Bass teaches a method of producing an addressable array of at least two different nucleic acid ligands covalently bonded to a surface of a substrate, said method comprising: (a) contacting blocked nucleoside monomers to at least a first location and a second location of a substrate surface displaying functional groups under conditions sufficient for said .blocked nucleoside monomers to covalently bond to said surface in said first and second locations to produce a substrate surface displaying covalently bound blocked monomers; (b) contacting said surface displaying blocked nucleoside monomers with an oxidation fluid to produce an oxidized surface; (c) contacting said oxidized surface with a deblocking fluid {deprotecting fluid}; (d) removing deblocking fluid from said deblocked surface by displacing said deblocking fluid from said surface with a wash fluid; and (e) reiterating steps (a) to (d) at least once to produce said addressable array having a first polymeric ligand at said first location of said substrate and a second polymeric ligand at said second location of said substrate (col. 1. line 55 to col. 2, lines 1-9 and 28-34 and Figures 1-3, which is identical to the Figures 1-3 of the instant invention).

Regarding claim 16, Bass et al teach the method of claim 1, wherein said blocked nucleoside monomers are contacted with said surface by pulse-jet deposition (col. 3, lines 61-67 and col. 7, lines 35-38).

Regarding claim 28, Bass et al teach the method according to claim 1, wherein said substrate is planar (col. 13, lines 2-5).

Claim Rejections - 35 USC § 103

5. Claims 2, 4-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bass as previously applied above in view of Anderson et al as previously applied in the previous Office action.

Regarding claims, Bass et al teach a method of producing an addressable array of at least two different nucleic acid ligands covalently bonded to a surface of a substrate, said method comprising contacting blocked nucleoside monomers to at least a first location and a second location of a substrate surface displaying functional groups under conditions sufficient for said .blocked nucleoside monomers to covalently bond to said surface in said first and second locations to produce a substrate surface displaying covalently bound blocked monomers; (b) contacting said surface displaying blocked nucleoside monomers with an oxidation fluid to produce an oxidized surface; (c) contacting said oxidized surface with a deblocking fluid; (d) removing deblocking fluid from said deblocked surface by displacing said deblocking fluid from said surface with a wash fluid; and (e) reiterating steps (a) to (d) at least once to produce said addressable array having a first polymeric ligand at said first location of said substrate and a second polymeric ligand at said second location of said substrate (col. 1. line 55 to col. 2, lines 1-9 and 28-34 and Figures 1-3, which is identical to the Figures 1-3 of the instant invention).

Bass does not provide any additional information on the wash fluid or deblocking fluid or wherein the method utilizes a flow cell.

Anderson et al disclose the method similar to that of Bass comprising contacting a blocked monomer at first and second locations having functional groups (e.g. cpg supports having the first monomer attached, Column 19, lines 55-58) under conditions sufficient for the monomer to covalently bond to the surface. Anderson et al further teach detritylation of the nucleotide with a blocking fluid; namely, step (i) of Table I (column 20), which generates an unblocked attached nucleoside nucleotide. Anderson et al further teach displacing the deblocking fluid with a purging fluid; namely, the solid supports are exposed to reagents sequentially wherein the reagents are kept separate based on density (column 5, lines 3-38 and column 6, lines 13-36) forming a liquid-liquid interface such that the solid support is not

exposed to a triple phase interface (column 12, lines 28-67 and Fig. 2A-2D). Anderson et al also teach the reacting of the unblocked attached nucleotide with another blocked nucleoside monomer; namely, coupling step ii of Table I (column 20); removing blocking groups to generate a function group and reiterating the steps to produce the array of at least two ligands (Column 19, line 55-Column 20, line 50). Anderson et al further teach the method wherein the solid supports are exposed to reagents sequentially wherein the reagents are kept separate based on density (Column 5, lines 3-38 and Column 6, lines 13-36) forming a liquid-liquid interface such that the solid support is not exposed to a triple phase interface (Column 12, lines 28-67 and Fig. 2A-2D).

With respect to claim 2, Anderson et al disclose the method wherein the sequentially applied liquids have a different density greater than zero (i.e. increasing density, Column 6, line 57-Column 7, line 14).

With respect to claim 4, Anderson et al wherein the washing fluid has a density that is lower than the density of the deblocking fluid (Column 5, lines 3-38 and Column 6, lines 13-36). In one embodiment, Anderson et al teach the deblocking (detritylation) fluid has a density that is greater than that of methylene chloride (i.e., 1.325 g/mL; column 21, lines 1-10). Detritylation is followed with a wash using acetonitrile, which has a density of 0.714 g/mL (Table II, step 3). Calculating the density difference using pure methyl chloride results in an Atwood number of 0.2996; a higher density deblocking fluid gives a higher Atwood number.

With respect to claim 5, Anderson et al disclose wherein the wash is a low viscosity (see col. 7, lines 68 to col. 8, line 1 and Table II, step 3 with discloses that the wash solution is acetonitrile).

With respect to claims 6 and 8, Anderson et al discloses wherein the wash fluid is acetronitrile (column 13, line 67-column 14, line 1), which has a low viscosity (col. 7, line 68 to col. 8, line 1). It is commonly known in the art base standard physical data that acetonitrile has a viscosity of 0.38 cp. Therefore, it is an inherent property that the wash fluid (acetonitrile) has a viscosity that does not exceed about 1.2 cP.

With respect to claim 7, Anderson et al disclose wherein said wash fluid is an organic fluid (Table II, step 3).

With respect to claim 9, Anderson et al disclose the method wherein displacing comprises flowing the subsequent liquid across the surface to produce a stratified liquid interface that moves across the surface (Column 12, lines 28-67 and Fig. 2A-2D).

With respect to claim 10, Anderson et al disclose a method of producing an array of at least two different polymeric ligands (e.g. oligonucleotides synthesized on control pore glass, the two different sequences being e.g. product and failed sequences, Column 20, lines 10-25) as previously discussed above. Anderson et al further teach the method wherein the steps are performed in a flow cell wherein the flow rate is controlled and monitored during passage of reagents (Column 5,lines 25-27; Column 14, lines 44-53 21). Anderson et al teach that it is important to control the flow rate because some synthesis steps take more or less time than other steps and because reagent waste resulting from excess use of reagents is expensive (Column 21, lines 30-65) but they are silent regarding specific flow rates. However, the reference clearly suggests that the flow rate is adjusted to maximize reagents and synthetic step. Therefore, It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to adjust the flow rate during the synthesis steps of Anderson to obtain optimal flow rates (e.g. about 1-20 cm/x). One of ordinary skill in the art would have been motivated to adjust the flow rate so as to maximize syntheses reaction with minimal waste of reagents as desired by Anderson et al (Column 21, lines 30-65).

With respect to claim 11, Anderson et al teach wherein the method comprises a sensing movement (rotation) that moves a stratified interface across the surface (column 12, lines 28-67 and Fig. 2A-2D).

With respect to claim 12-14, Anderson et al disclose the method wherein the steps are preformed in a flow cell i.e. internal space for fluid flow so as to contact solid support (Column 5, lines 20-38).

With respect to claim 15, Anderson et al disclose the method wherein said surface is contacted with a capping liquid prior to said deblocking (Column 13, line 59-Column 14, line 11 and Column 19, line 55-Column 20, line 50).

The claims 2 and 4-15 merely recite a plethora of manipulation reagents and methodologies, as well as routine optimization or reaction components, concentrations, and parameters. Clearly such conventional and trivial modification and optimizations do not contribute towards patentability. Thus, one of ordinary skill in the art would have been motivated to modify the method of Bass et al with the reagents of Anderson in the manner of the claims to achieve the expected benefits, optimizations an/or expanded applications. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods with a reasonable expectation of success.

Response to Arguments

6. Applicant traverses the rejection of Bass et al on the grounds that the reference does not teach the displacement steps (d and h). Applicant states that the cited passages of the rejection merely list the steps of *in situ* fabrication, but do not teach displacing the blocking fluid with a wash fluid.

Applicant traverses the rejection of Bass et al in view of Anderson et al on the grounds that the proposed combination would either change the principle of the operation of the methods taught by the references or render them inoperable. Applicant states that if one would combine the teachings of Bass and that of Anderson, one would end up having an addressable array inside an enclosed rotor. Applicant states that since a glass bead is not an addressable array nor can be an addressable array exists in suspension, it would render either Bass's method or Anderson's method inoperable. Applicant asserts that an operable modification would not contain the element of fluid displacement in a rotor or column taught by Anderson since it would be inoperable as described above.

7. All of the arguments have been thoroughly reviewed ad considered but are not found persuasive. In response to Applicant's arguments that Bass does not teach the displacement steps (d and h), it is noted that Bass et al expressly teach performing one

or more intermediate washing steps (e.g., col. 2). With regards to displacing or removing the deblocking solution, this limitation is inherent in the washing step as it is obvious that washing the addressable array will result in displacing any fluid that may present thereon.

8. In response to Applicant's arguments that that the combination of Bass et al in view of Anderson et al would render an inoperable invention, it is noted that Anderson was not cited for any suspension inside of a rotor during fluid displacement. Rather, the secondary reference of Anderson was cited for its teachings of the type of washing fluid and the type of blocking fluid which can be used in preparing an array comprising blocked monomers as well as the use of a flow cell. The use of a rotor as argued by Applicant does not effect, modify or hinder the function of the washing fluid or deblocking fluid or flow cell or prevent the fluids and flow cell from functioning effectively in the method of producing an addressable array as taught by Bass et al. Further, the use of the washing fluid and deblocking fluid and flow cell as taught by Anderson does not make the addressable array of Bass inoperative because the prior art and Anderson recognizes that the compositions (fluids) taught by Anderson can be used effectively and predictably as a washing agent or blocking agent in monomer attachment to a surface. Applicant's arguments are not sufficient to overcome the prior art rejections noted above.

Conclusion

9. No claims are allowed. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CYNTHIA B. WILDER whose telephone number is (571)272-0791. The examiner can normally be reached on a flexible schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/CBW/

/GARY BENZION/
Supervisory Patent Examiner, Art Unit 1637